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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,500	09/26/2005	Eberhard Amtmann	099380.B270041	7509

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EXAMINER	
WEBB, WALTER E	
ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,500	AMTMANN ET AL.	
	Examiner	Art Unit	
	WALTER E. WEBB	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,10 and 12-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9, 10 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 10/30/2008, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112--previous

Claim 9 remains rejected under 35 U.S.C. 112, first paragraph. This rejection also applies to newly amended claim 14.

Applicant has amended claim 9 to recite treatment of “a solid tumor”, which is narrower than cancerous disease. However, “solid tumor” still represents a very broad genus. Given the unpredictability in the art with regard to treating cancer, it is doubtful that applicant's invention as claimed is enabled for treating solid tumors in general.

Applicant argues that the claimed compounds have a particular effectiveness in the acidic environment of tumor tissues and that the claimed compounds overcome the deficiencies of cisplatin compounds. However, applicant’s data shows cytotoxic activity *in vitro* in two cancer cell lines (lung and melanoma) with seven compounds. The compounds cover where R is C1-6, and where R is cyclohexyl. These results are not necessarily predictive of other extremely different compounds where R is C30 or a polycyclic alkyl residue of 30 carbon atoms. Applicant provides no reasonable basis for predicting the success of these other compounds.

Applicant also tested one compound (Bis(O-isopropyl-dithiocarbanato)Pd(II) in a mouse with human small lung cancer cells, and cyclohexyl-palladium xanthate in vitro with glioma, bladder, lung, melanoma, breast, and ovary cell lines. However, more guidance is needed in terms of predicting the success of the myriads of other compounds and tumor types not tested. Since the art recognizes limitations in treatment even where the compound treats a broad spectrum of cancers, the artisan would not expect applicant's compounds to be able to treat solid tumors in general.

Applicant argues that since all tested compounds showed marked anti-tumor activity, it would be routine for a person of ordinary skill in the art to synthesize other compounds and test them for anti-tumor activity. However, 35 USC 112, first paragraph, protects the artisan from this type of hit or miss experimentation. It is well known that slight changes in a compound can result in significant effects. For example, applicant's data at page 13 (Table 1) shows that Bis(O-isopropyl-dithiocarboanato)platin is twice as cytotoxic to CALU-6 over Bis(O-ethyl-dithiocarboanato)platin at pH 6.8. Since slight variations may have significant effects on the function of a compound, it would not be reasonable to predict that a compound of applicant's invention where R is C1 would behave similarly with a compound where R is a polycyclic alkyl residue of 30 carbon atoms. The artisan would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention. Accordingly, claim 9 remains rejected.

112 Indefiniteness--New

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites the limitation "the cancerous disease" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102--previous

The rejection of claims 1-4, 7 and 12 rejected under 35 USC 102(b) as being anticipated by Watt et al. is maintained. This rejection also applies to newly amended claims 16 and 17.

Applicant argues that Watt et al. does not disclose that the compounds are dissolved in ethanol, but that the technical grade potassium ethylxanthate, which was used to form the compounds, was recrystalized form ethanol. The Examiner agrees. However, at page 899 H_2O is used as the solvent for the reaction, and H_2O suffices as a pharmaceutically compatible diluent. (See lines 5-8.)

In regard to claims 16 and 17, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Since

the prior art compound of Watt et al. is not structurally different from the claimed invention, it capable of exhibiting a higher cytotoxic activity against human cancer cells at pH 6.8 than at pH 7.4, including where the human cancer cell is SK_MEL 25 or CALU-6.

Claim Rejections - 35 USC § 103--previous

Claims 5, 6 and 9-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Watt et al. as applied to claims 1-4, 7, 12, 16 and 17 above, in view of Amtmann et al., and in further view of Das et al. This rejection also applies to newly amended claims 13-15.

Applicant argues that the claimed compounds have higher cytotoxic activity at a slightly acidic pH than in the alkaline range. Applicant states that because of this, a person of ordinary skill in the art would not have been motivated to replace the platinum in the complexes with palladium. However, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. MPEP 2144. Therefore it is not necessary for the prior art to teach the pH dependent activity in order to arrive at the instant invention. Das provides motivation for replacing the platinum with palladium insofar as it teaches that palladium complexes are better cytotoxic agents when compared with platinum complexes.

Applicant argues that Das is limited to blood cancer and fails to provide any reasonable expectation that palladium complexes would have a pH dependent anti-tumor activity and should be suitable for treatment of solid tumors. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. Das was used to provide motivation for replacing the platinum of Amtmann with palladium. Amtmann provides motivation for treating solid tumors.

Applicant also argues that the Schiff base ligands taught by Das are not sufficienty structurally similar such that a person skilled in the art would have expected them to have similar properties. However, Das is not necessarily relied upon for structural similarity. The reference teaches that the type of metal used can pose a significant advantage in the treatment of cancer and that palladium chelates are more likely to be effective anti-tumor agents than chelates of other metals.

Applicant argues, based on Salim Abu-Surrah et al., that a person of ordinary skill in the art would not have reasonably expected that palladium complexed with xanthate, which does not have a nitrogen ligand, would be suitable as an anti-tumor agent, because of the different ligand-exchange kinetics between platinum and palladium complexes. However, the rejection is based on the combined teachings of Watt, Amtmann, and Das. Given these teachings the artisan would reasonably expect success in administering the compound(s) of Amtmann substituted with palladium. The artisan would not necessarily rely on nitrogen ligands for success since Das states that the palladium chelates are effective anti-tumor agents “at least with sulphur donor

atoms." Because the xanthates of Amtmann have sulphur donor atoms the artisan would reasonably expect success in substituting the platinum with palladium.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612